



Clinical trial results:

A Phase 2, Randomized, Double-blind, Placebo-controlled, 6-Week, Parallel-design Study of the Efficacy and Safety of VX-150 in Treating Subjects With Pain Caused by Small Fiber Neuropathy

Summary

EudraCT number	2017-001042-10
Trial protocol	DE NL IT
Global end of trial date	08 November 2018

Results information

Result version number	v2 (current)
This version publication date	13 December 2021
First version publication date	27 November 2019
Version creation reason	• New data added to full data set Secondary endpoints data will be added

Trial information

Trial identification

Sponsor protocol code	VX16-150-102
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Additional study identifiers

ISRCTN number	-
ClinicalTrials.gov id (NCT number)	NCT03304522
WHO universal trial number (UTN)	-

Notes:

Sponsors

Sponsor organisation name	Vertex Pharmaceuticals Incorporated
Sponsor organisation address	50 Northern Avenue, Boston, Massachusetts, United States,
Public contact	Medical Monitor, Vertex Pharmaceuticals Incorporated, +1 617 341 6777, medicalinfo@vrtx.com
Scientific contact	Medical Monitor, Vertex Pharmaceuticals Incorporated, +1 617 341 6777, medicalinfo@vrtx.com

Notes:

Paediatric regulatory details

Is trial part of an agreed paediatric investigation plan (PIP)	No
Does article 45 of REGULATION (EC) No 1901/2006 apply to this trial?	No
Does article 46 of REGULATION (EC) No 1901/2006 apply to this trial?	No

Notes:

Results analysis stage

Analysis stage	Final
Date of interim/final analysis	05 December 2018
Is this the analysis of the primary completion data?	Yes
Primary completion date	12 October 2018
Global end of trial reached?	Yes
Global end of trial date	08 November 2018
Was the trial ended prematurely?	No

Notes:

General information about the trial

Main objective of the trial:

To evaluate the efficacy of VX-150 for the treatment of pain caused by small fiber neuropathy.

Protection of trial subjects:

The study was conducted in accordance with the ethical principles stated in the Declaration of Helsinki and the International Council on Harmonization (ICH) Guideline for Good Clinical Practice (GCP).

Background therapy: -

Evidence for comparator: -

Actual start date of recruitment	20 September 2017
Long term follow-up planned	No
Independent data monitoring committee (IDMC) involvement?	Yes

Notes:

Population of trial subjects

Subjects enrolled per country

Country: Number of subjects enrolled	Italy: 10
Country: Number of subjects enrolled	Netherlands: 6
Country: Number of subjects enrolled	United States: 71
Country: Number of subjects enrolled	Germany: 2
Worldwide total number of subjects	89
EEA total number of subjects	18

Notes:

Subjects enrolled per age group

In utero	0
Preterm newborn - gestational age < 37 wk	0
Newborns (0-27 days)	0
Infants and toddlers (28 days-23 months)	0
Children (2-11 years)	0
Adolescents (12-17 years)	0
Adults (18-64 years)	66
From 65 to 84 years	23
85 years and over	0

Subject disposition

Recruitment

Recruitment details: -

Pre-assignment

Screening details:

A total of 89 subjects were enrolled and randomized in the study.

Period 1

Period 1 title	Overall Trial (overall period)
Is this the baseline period?	Yes
Allocation method	Randomised - controlled
Blinding used	Double blind
Roles blinded	Subject, Investigator, Carer, Assessor

Arms

Are arms mutually exclusive?	Yes
Arm title	VX-150

Arm description:

Subjects received VX-150 once daily for 6 weeks.

Arm type	Experimental
Investigational medicinal product name	VX-150
Investigational medicinal product code	
Other name	
Pharmaceutical forms	Capsule
Routes of administration	Oral use

Dosage and administration details:

Subjects received VX-150 1250 milligrams (mg) once daily.

Arm title	Placebo
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Arm description:

Subjects received placebo matched to VX-150 once daily for 6 weeks.

Arm type	Placebo
Investigational medicinal product name	Placebo (matched to VX-150)
Investigational medicinal product code	
Other name	
Pharmaceutical forms	Capsule
Routes of administration	Oral use

Dosage and administration details:

Subjects received placebo matched to VX-150 once daily.

Number of subjects in period 1	VX-150	Placebo
Started	46	43
Completed	45	35
Not completed	1	8
Other	-	1

Withdrawal of consent (for other reason)	-	2
Adverse event	-	4
Withdrawal of consent (due to lack of efficacy)	1	1

Baseline characteristics

Reporting groups

Reporting group title	VX-150
Reporting group description:	
Subjects received VX-150 once daily for 6 weeks.	
Reporting group title	Placebo
Reporting group description:	
Subjects received placebo matched to VX-150 once daily for 6 weeks.	

Reporting group values	VX-150	Placebo	Total
Number of subjects	46	43	89
Age categorical Units: Subjects			
Age continuous Units: years			
arithmetic mean	55.1	58.1	-
standard deviation	± 12.34	± 11.86	-
Gender categorical Units: Subjects			
Female	22	21	43
Male	24	22	46
Ethnicity (NIH/OMB) Units: Subjects			
Hispanic or Latino	3	5	8
Not Hispanic or Latino	43	38	81
Unknown or Not Reported	0	0	0
Race (NIH/OMB) Units: Subjects			
American Indian or Alaska Native	0	0	0
Asian	0	1	1
Native Hawaiian or Other Pacific Islander	0	0	0
Black or African American	6	4	10
White	39	34	73
More than one race	1	2	3
Unknown or Not Reported	0	2	2
Pain Intensity at Baseline on 11-point Numeric Rating Scale (NRS)			
Pain intensity was evaluated using the 11-point NRS (where 0 signified no pain and 10 signified worst imaginable pain). Higher score indicates greater level of pain. Baseline score was average of daily pain scores from Day -7 to Day -1.			
Units: units on a scale			
arithmetic mean	6.433	5.990	-
standard deviation	± 1.440	± 1.413	-

End points

End points reporting groups

Reporting group title	VX-150
Reporting group description:	
Subjects received VX-150 once daily for 6 weeks.	
Reporting group title	Placebo
Reporting group description:	
Subjects received placebo matched to VX-150 once daily for 6 weeks.	

Primary: Change in Weekly Average of Daily Pain Intensity on the 11 Point NRS

End point title	Change in Weekly Average of Daily Pain Intensity on the 11 Point NRS
End point description:	
Pain intensity was evaluated using the 11-point NRS (where 0 signified no pain and 10 signified worst imaginable pain) during the last 24 hours on the NRS each evening. Higher score indicates greater level of pain. Full Analysis Set (FAS) included all randomized subjects who received at least 1 dose of study drug.	
End point type	Primary
End point timeframe:	
From Baseline at Week 6	

End point values	VX-150	Placebo		
Subject group type	Reporting group	Reporting group		
Number of subjects analysed	46	43		
Units: units on a scale				
least squares mean (standard error)	-2.018 ($\pm$ 0.274)	-0.933 ($\pm$ 0.287)		

Statistical analyses

Statistical analysis title	Statistical Analysis
Comparison groups	VX-150 v Placebo
Number of subjects included in analysis	89
Analysis specification	Pre-specified
Analysis type	superiority
P-value	< 0.0001
Method	Mixed-effects Model for Repeated Measure
Parameter estimate	LS Mean Difference
Point estimate	-1.085

Confidence interval	
level	95 %
sides	2-sided
lower limit	-1.876
upper limit	-0.293

Secondary: Percentage of Subjects With Greater Than or Equal to ($\geq$) 30 Percent (%) Reduction in the Weekly Average of Daily Pain Intensity on the 11-Point NRS

End point title	Percentage of Subjects With Greater Than or Equal to ($\geq$) 30 Percent (%) Reduction in the Weekly Average of Daily Pain Intensity on the 11-Point NRS
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End point description:

Pain intensity was evaluated using the 11-point NRS (where 0 signified no pain and 10 signified worst imaginable pain) during the last 24 hours on the NRS each evening. Higher score indicates greater level of pain. Percentage of subjects $\geq$ 30% reduction in the weekly average of daily pain intensity on the 11-Point NRS were reported. FAS. Here, 'number of subjects analysed' signifies subjects who were evaluable for this endpoint.

End point type	Secondary
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End point timeframe:

From Baseline at Week 6

End point values	VX-150	Placebo		
Subject group type	Reporting group	Reporting group		
Number of subjects analysed	40	34		
Units: percentage of subjects				
number (not applicable)	45.0	26.5		

Statistical analyses

No statistical analyses for this end point

Secondary: Percentage of Subjects With $\geq$ 50% Reduction in the Weekly Average of Daily Pain Intensity on the 11-Point NRS

End point title	Percentage of Subjects With $\geq$ 50% Reduction in the Weekly Average of Daily Pain Intensity on the 11-Point NRS
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End point description:

Pain intensity was evaluated using the 11-point NRS (where 0 signified no pain and 10 signified worst imaginable pain) during the last 24 hours on the NRS each evening. Higher score indicates greater level of pain. Percentage of subjects $\geq$ 50% reduction in the weekly average of daily pain intensity on the 11-Point NRS were reported. FAS. Here, 'number of subjects analysed' signifies subjects who were evaluable for this endpoint.

End point type	Secondary
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End point timeframe:

From Baseline at Week 6

End point values	VX-150	Placebo		
Subject group type	Reporting group	Reporting group		
Number of subjects analysed	40	34		
Units: percentage of subjects				
number (not applicable)	32.5	17.6		

Statistical analyses

No statistical analyses for this end point

Secondary: Change in the Daily Sleep Interference Scale (DSIS)

End point title	Change in the Daily Sleep Interference Scale (DSIS)
End point description:	
Pain-associated sleep interference was assessed using DSIS, based on an 11-point scale (where 0 signified none: pain does not interfere with sleep and 10 signified severe: pain completely interferes with sleep, unable to sleep). Higher score indicates greater pain associated sleep interference. FAS.	
End point type	Secondary
End point timeframe:	
From Baseline at Week 6	

End point values	VX-150	Placebo		
Subject group type	Reporting group	Reporting group		
Number of subjects analysed	46	43		
Units: units on a scale				
least squares mean (standard error)	-1.777 ($\pm$ 0.276)	-0.665 ($\pm$ 0.289)		

Statistical analyses

Statistical analysis title	VX-150 vs Placebo
Comparison groups	VX-150 v Placebo
Number of subjects included in analysis	89
Analysis specification	Pre-specified
Analysis type	superiority
P-value	< 0.0001
Method	Mixed-effects Model for Repeated Measure
Parameter estimate	LS Mean Difference
Point estimate	-1.111

Confidence interval	
level	95 %
sides	2-sided
lower limit	-1.911
upper limit	-0.312

Secondary: Percentage of Subjects Categorized as Improved on the Patient Global Impression of Change (PGIC) Scale

End point title	Percentage of Subjects Categorized as Improved on the Patient Global Impression of Change (PGIC) Scale
End point description:	
PGIC scale evaluated the change in activity limitations, symptoms, emotions, and overall quality of life (QoL) related to the subjects painful condition on 7-point scale from 1 (improved) to 7 (worse). Subjects were categorized as following: scale from 1 - 2 were categorized as "improved", scale from 3 - 4 as "no change" and scale from 5 - 7 were categorized as "worse". Percentage of subjects categorized as improved on PGIC scale at week 6 were reported for this outcome measure. FAS. Here, 'number of subjects analysed' signifies subjects who were evaluable for this endpoint.	
End point type	Secondary
End point timeframe:	
At Week 6	

End point values	VX-150	Placebo		
Subject group type	Reporting group	Reporting group		
Number of subjects analysed	46	43		
Units: percentage of subjects				
number (not applicable)	39.5	13.5		

Statistical analyses

No statistical analyses for this end point

Secondary: Change in Pain Intensity on the 11-Point NRS

End point title	Change in Pain Intensity on the 11-Point NRS
End point description:	
Pain intensity was evaluated using the 11-point NRS (where 0 signified no pain and 10 signified worst imaginable pain) during the last 24 hours on the NRS each evening. Higher score indicates greater level of pain. FAS.	
End point type	Secondary
End point timeframe:	
From Baseline at Week 6	

End point values	VX-150	Placebo		
Subject group type	Reporting group	Reporting group		
Number of subjects analysed	46	43		
Units: units on a scale				
least squares mean (standard error)	-18.4 (± 3.1)	-5.0 (± 3.1)		

Statistical analyses

Statistical analysis title	VX-150 vs Placebo
Comparison groups	Placebo v VX-150
Number of subjects included in analysis	89
Analysis specification	Pre-specified
Analysis type	superiority
P-value	< 0.0001
Method	Mixed-effects Model for Repeated Measure
Parameter estimate	LS Mean Difference
Point estimate	-0.6
Confidence interval	
level	95 %
sides	2-sided
lower limit	-1.5
upper limit	0.3

Secondary: Pre-dose Plasma Concentration (Ctough) of VRT-1207355 and the Metabolite VRT-1268114

End point title	Pre-dose Plasma Concentration (Ctough) of VRT-1207355 and the Metabolite VRT-1268114 ^[1]
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End point description:

Pharmacokinetic (PK) set included subjects who received at least 1 dose of study drug and for whom the primary PK data was considered to be sufficient and interpretable.

End point type	Secondary
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End point timeframe:

Pre-dose at Day 7

Notes:

[1] - The end point is not reporting statistics for all the arms in the baseline period. It is expected all the baseline period arms will be reported on when providing values for an end point on the baseline period. Justification: This endpoint was applicable for VX-150 arm. Therefore, data are reported for this arm only.

End point values	VX-150			
Subject group type	Reporting group			
Number of subjects analysed	12			
Units: microgram per milliliter (mcg/mL)				
arithmetic mean (standard deviation)				
VRT-1207355	3.89 (± 2.73)			
VRT-1268114	1.35 (± 0.752)			

Statistical analyses

No statistical analyses for this end point

Secondary: Number of Subjects With Clinically Meaningful Findings in Columbia Suicide Severity Rating Scale (C-SSRS) Responses

End point title	Number of Subjects With Clinically Meaningful Findings in Columbia Suicide Severity Rating Scale (C-SSRS) Responses
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End point description:

The C-SSRS is an interview-based rating scale was evaluated through a series of questions about suicidal thoughts and behaviors with the possible answers yes or no. Yes represents a worse outcome. Clinically Meaningfulness of C-SSRS responses were judged by investigator based on answers received from subjects. Here "99999" represents that no subject had any clinically meaningful findings in C-SSRS responses. Safety Set included all subjects who have received at least 1 dose of study drug.

End point type	Secondary
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End point timeframe:

Day 1 up to Week 10

End point values	VX-150	Placebo		
Subject group type	Reporting group	Reporting group		
Number of subjects analysed	46	43		
Units: subjects	99999	99999		

Statistical analyses

No statistical analyses for this end point

Secondary: Safety and Tolerability as Assessed by Number of Subjects With Treatment-Emergent Adverse Events (AEs) and Serious Adverse Events (SAEs)

End point title	Safety and Tolerability as Assessed by Number of Subjects With Treatment-Emergent Adverse Events (AEs) and Serious Adverse Events (SAEs)
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End point description:

End point type	Secondary
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End point timeframe:

Day 1 up to Week 10

End point values	VX-150	Placebo		
Subject group type	Reporting group	Reporting group		
Number of subjects analysed	46	43		
Units: subjects				
Subjects with AEs	29	24		
Subjects with SAEs	0	3		

Statistical analyses

No statistical analyses for this end point

Adverse events

Adverse events information

Timeframe for reporting adverse events:

Day 1 up to Week 10

Assessment type	Systematic
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Dictionary used

Dictionary name	MedDRA
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Dictionary version	21.1
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Reporting groups

Reporting group title	Placebo
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Reporting group description:

Subjects received placebo matched to VX-150 once daily for 6 weeks.

Reporting group title	VX-150
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Reporting group description:

Subjects received VX-150 once daily for 6 weeks.

Serious adverse events	Placebo	VX-150	
Total subjects affected by serious adverse events			
subjects affected / exposed	3 / 43 (6.98%)	0 / 46 (0.00%)	
number of deaths (all causes)	0	0	
number of deaths resulting from adverse events			
Injury, poisoning and procedural complications			
Tendon rupture			
subjects affected / exposed	1 / 43 (2.33%)	0 / 46 (0.00%)	
occurrences causally related to treatment / all	0 / 1	0 / 0	
deaths causally related to treatment / all	0 / 0	0 / 0	
Cardiac disorders			
Atrial fibrillation			
subjects affected / exposed	1 / 43 (2.33%)	0 / 46 (0.00%)	
occurrences causally related to treatment / all	0 / 1	0 / 0	
deaths causally related to treatment / all	0 / 0	0 / 0	
Infections and infestations			
Diverticulitis			
subjects affected / exposed	1 / 43 (2.33%)	0 / 46 (0.00%)	
occurrences causally related to treatment / all	0 / 1	0 / 0	
deaths causally related to treatment / all	0 / 0	0 / 0	

Frequency threshold for reporting non-serious adverse events: 5 %

Non-serious adverse events	Placebo	VX-150	
Total subjects affected by non-serious adverse events			
subjects affected / exposed	7 / 43 (16.28%)	16 / 46 (34.78%)	
Nervous system disorders			
Headache			
subjects affected / exposed	5 / 43 (11.63%)	11 / 46 (23.91%)	
occurrences (all)	6	14	
Gastrointestinal disorders			
Dry mouth			
subjects affected / exposed	1 / 43 (2.33%)	3 / 46 (6.52%)	
occurrences (all)	1	3	
Nausea			
subjects affected / exposed	1 / 43 (2.33%)	3 / 46 (6.52%)	
occurrences (all)	1	3	
Musculoskeletal and connective tissue disorders			
Arthralgia			
subjects affected / exposed	1 / 43 (2.33%)	3 / 46 (6.52%)	
occurrences (all)	1	3	
Muscle spasms			
subjects affected / exposed	0 / 43 (0.00%)	3 / 46 (6.52%)	
occurrences (all)	0	3	

More information

Substantial protocol amendments (globally)

Were there any global substantial amendments to the protocol? Yes

Date	Amendment
21 April 2017	Amended inclusion criteria to clarify the study population and Body Mass Index (BMI)
19 May 2017	Amended the dose limit of VX-150
11 August 2017	Allowed inclusion of women of childbearing potential; updated the upper limit of BMI and the visit requirements
13 April 2018	Updated inclusion and exclusion criteria to facilitate subject recruitment
25 May 2018	The protocol was amended to enable timely assessment of study data to support continued development

Notes:

Interruptions (globally)

Were there any global interruptions to the trial? No

Limitations and caveats

None reported